UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,602	01/09/2007	Ji Sook Park	1751-409	3620

6449 7590 02/24/2009

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
02/24/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/581,602	PARK ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/9/07, 10/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The contents of the Application, including claims, specification, and drawings, were received on 6/5/06 and have been entered into the record.

2. Claims 1-5 are pending and are the subject of this office action.

Information Disclosure Statement

1. The information disclosure statement received on 1/9/07 has been fully considered.

2. The information disclosure statement received on 10/28/08 has been considered. Citation 1 has been considered only in view of pages 24-32, as these are the only pages of the reference which are written in English.

Claim Objections

The Examiner suggests the syntax of claim 4 can be improved by amending the claim to recite "with an ultrafiltration membrane with a molecular cut-off of 10,000". It is also suggested to amend the claim to specify the appropriate molecular weight units (e.g. kDa, daltons, etc).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the process of claim 1, wherein the solution is subjected to diafiltration with an ultrafiltration membrane of molecular weight cut-off of 10,000. However, the claim does not recite any units, and thus it is not clear if the molecular weight cut-off is 10,000 daltons, kDa, or some other unit.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Utsumi *et al* ("Utsumi" – *Eur. J. Biochem.*, 1989, Vol. 181, p. 545-553), in view of Carter *et al* ("Carter" – US 4,483,849), and further in view of Revel *et al* ("Revel" - US 4,808,523). Carter and Revel were cited in the IDS received on 1/9/2007.

The claims of the instant invention are drawn to a process for purifying human interferon beta (IFN-β) from a recombinant IFN-β-containing culture, wherein said method comprises performing affinity chromatography and reverse-phased high-performance liquid chromatography (RP-HPLC). The claims are further drawn to methods of affinity chromatography comprising washing with various buffer solutions comprising a range of propylene glycol concentrations and at cited ranges of pH, wherein said buffers further comprise sodium chloride, and wherein said buffers comprise sodium or potassium phosphate. Also claimed is said process for purifying IFN-β, wherein said process further comprises ultrafiltration of the solution obtained by affinity chromatography with an ultrafiltration membrane of molecular weight cut-off of 10,000, and subsequently loading an IFN-β-containing fraction on an RP-HPLC column.

Utsumi teaches a method of purifying human recombinant IFN-β from culture fluid, wherein said method comprises loading said IFN-β-containing cell culture fluid onto an affinity column (blue Sepharose CL-6B), followed by washing and elution with a 20 mM phosphate buffer, pH 7.4, and further affinity purification using a column of anti-IFN-β-specific antibody. The resulting solution was then further purified by RP-HPLC (see p. 546, 1st column – "Purification of HuIFN-β1s"). Uttsumi is silent regarding the use of propylene glycol-containing buffers.

However, Carter discloses a method of purifying IFN-β comprising affinity chomatography using propylene glycol-containing buffers (see Example 1; see also claims 1-5). Specifically, Carter teaches purification of IFN-β-containing fluid using an equilibrated Affi-Gel Blue column, which is taught by the present specification to be an affinity purification column (see paragraphs 0090-0011). Carter also discloses washing and elution with sodium phosphate buffers containing 40-50% propylene glycol (see

Example 1, 2nd paragraph). Carter specifically teaches that solutions containing ethylene glycol are toxic, and therefore the use of ethylene glycol is not desirable in the purification of therapeutic agents. In contrast, propylene glycol is not toxic and also yields higher concentrations of IFN-β when used in methods of purification (column 1, line 25 - column 2, line 52).

Similarly, Revel also teaches purification of recombinant human IFN-β by affinity chromatography using a Blue-Sepharose column, followed by elution with 20 mM phosphate buffer, pH 7, containing 40% propylene glycol (see column 13, line 60 - column 14, line 17; see also claims 2, 7, and 8). Revel also teaches concentration of affinity-purified IFN-β by ultrafiltration with a YM10 membrane, which is known in the art to have a molecular weight cut-off of 10,000 daltons (see Millipore catalog - http://www.millipore.com/catalogue/itemdetail.do?id=13622 – this citation is not being used in a grounds of rejection, but to point out a physical property of YM10 ultrafiltration membranes). Although the present claims only require an ultrafiltration membrane with a molecular weight cut-off of 10,000 and does not explicitly recite any units, claim 4 has been interpreted as reading on a membrane with a cut-off of 10,000 daltons.

Therefore, one of ordinary skill in the art, at the time the instant invention was conceived, would have been motivated to practice a process of IFN-β purification that is commensurate in scope with the present claims by following the combined teachings of Utsumi, Carter, and Revel. The motivation to do so comes from the disclosure of Utsumi, which teaches purification of IFN-β by a method comprising affinity chromatography followed by further RP-HPLC purification. Further motivation comes from both Carter and Revel, which teach purification of IFN-β by affinity chromatography using buffers containing propylene glycol, and the specific teaching by Carter that propylene glycol is a preferable component of such purification methods by virtue of being non-toxic because such use leads to higher yields of IFN-β (see Carter). Therefore, one of ordinary skill in the art would be motivated to practice the method of Utsumi using the propylene glycol-containing buffers of Carter or Revel because a skilled artisan would know that IFN-β can be purified by the method of Utsumi, and that the incorporation of propylene glycol, as taught by both Carter and Revel, would lead to more efficient purification and ultimately a safer therapeutic agent. Further, by teaching concentration of purified IFN-β using an ultrafiltration membrane, Revel provides the motivation to further concentrate the affinity-purified IFN-β prior to RP-HPLC purification.

Finally, although neither Carter nor Revel disclose all of the exact claimed propylene glycol concentration ranges, it is noted that both Carter and Revel provide the motivation to use propylene glycol-containing buffers, as discussed above, and also teach buffers containing 40-50% propylene

glycol, which is encompassed by some of the claimed ranges. Thus, one of ordinary skill in the art would have both the motivation and the ability to optimize the concentration of propylene glycol in the buffers of either Carter or Revel. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of the present claims, namely purification of IFN-β by affinity chromatography followed by RP-HPLC and the use of propylene glycol-containing buffers used with the affinity chromatography, are disclosed in the prior art, it would not be inventive to optimize the concentrations of propylene glycol.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 10/581,597. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to a process for purifying IFN-β comprising affinity purification and either RP-HPLC ('602) or cation exchange chromatography ('597). Although the present application is drawn to methods of affinity chromatograph and RP-HPLC, the specification of the present application discloses

that cation exchange chromatography is also a method for purification of IFN-β. Similarly, although the '597 application is drawn to method of affinity chromatography and cation exchange chromatograph, the specification of the '597 application teaches that RP-HPLC can be used to purify IFN-β. Therefore, because both applications teach purification of IFN-β via affinity chromatograph and either RP-HPLC or cation exchange chromatography, a person of ordinary skill in the art would conclude that the subject matter of the present application overlaps with that of the '597 application..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong

Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647